Imaging

ROLE OF EICOSANOIDS IN REGULATING CAPILLARY PERFUSION: EVALUATION OF CAPILLARY BLOOD VOLUME WITH CONTRAST ULTRASOUND

Poster Contributions
Poster Sessions, Expo North
Sunday, March 10, 2013, 9:45 a.m.-10:30 a.m.

Session Title: Imaging: Echo - Contrast Echocardiography/Vascular Imaging
Abstract Category: 18. Imaging: Echo
Presentation Number: 1225-326

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Background: Contrast-enhanced ultrasound (CEU) can quantify tissue capillary blood volume (CBV). This technique has been used to study functional control of capillaries in response to metabolic stimuli. Increases in muscle CBV in response to insulin are partially regulated by nitric oxide (NO) release. However other mediators of capillary recruitment have not been identified. We hypothesized that epoxyeicosatrienoic acids (EETs), which are vasodilating endothelial-derived hyperpolarizing factors, are regulators of muscle CBV and perfusion.

Methods: We studied 10 lean rats, 5 wild-type mice and 8 insulin-resistant db/db mice. Skeletal muscle CBV, microvascular flux rate, and muscle blood flow (MBF) were derived from CEU microbubble destruction replenishment data. Studies were performed at baseline and after administration of tAUCB (1 mg/kg) which is an inhibitor of soluble epoxide hydrolase (sEH) that enzymatically degrades EETs. Studies were performed at 30 min intervals for 2 hr in rats, and at 15 min intervals for 1 hr in mice. In 5 rats, L-NAME infusion was initiated 30 min prior to tAUCB to evaluate whether effects were independent of NO.

Results: In wild-type mice tAUCB increased skeletal muscle CBV by 40% ($p<0.05$) without change in BP. There was a concomitant increase in capillary blood flux rate, producing a 150% increase in MBF. Although CBV was lower at baseline in db/db than in wild-type mice, tAUCB produced an even greater proportional increase in CBV. In rats, tAUCB produced a 27% increase in CBV ($p<0.05$). Maximal CBV occurred early (at 30 min) in both species and remained constant thereafter. CBV decreased by 13% after pretreatment with L-NAME and then subsequently increased by 19% ($p<0.05$) after tAUCB.

Conclusions: We conclude that the EET family of endothelial-derived hyperpolarizing factors participate in the regulation of functional capillary density. The effects of EETs are independent of NO. Pharmacologic increase in EETs with sEH-inhibitors may provide a new approach to treating diseases such as insulin resistance where there is inadequate capillary response to metabolic stimuli.